

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claims 1-18 are canceled.

19. (new): A cell targeting conjugate comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

a DNA minor groove binding ligand incorporating an effective Auger electron-emitting and/or gamma-emitting and/or positron-emitting atom or photoactive moiety;

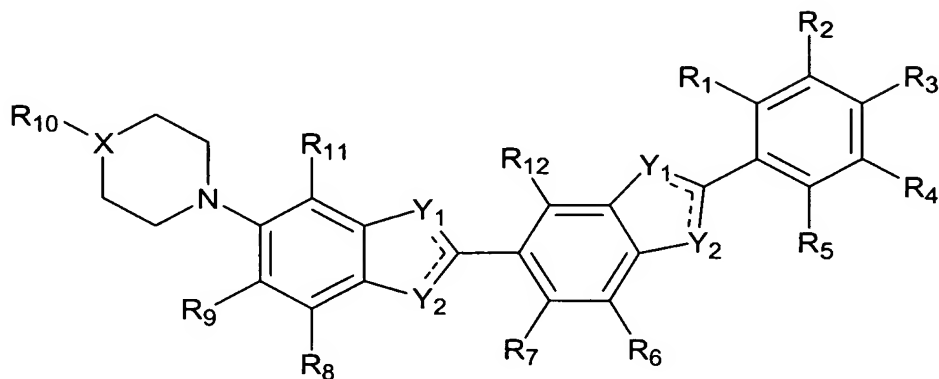
a target cell specific protein or peptide that is capable of internalisation by target cells;

wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

20. (new): The cell targeting conjugate according to claim 19 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

21. (new): The cell targeting conjugate according to claim 19 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbix), BrE-3, murine A7, C50, humanized MN-14, anti-A33, MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10), Campath-1H, N901, Ep2, somatostatin analogues, tositumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

22. (new): The cell targeting conjugate according to claim 19 wherein the cell targeting conjugate is represented by Formula (I), wherein:



Formula (I)

X is carbon or nitrogen;

Y₁ and Y₂ are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y₁ and Y₂ are not both either C(R') or nitrogen;

--- is a double bond unless the attached Y₁ or Y₂ is N(R'), oxygen or sulfur in which case it is a single bond;

R₁ to R₁₂ are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R₁ to R₅ may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R₁

to R₁₂ comprises a target cell specific protein or peptide, and wherein at least one other of R₁ to R₁₂ comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

23. (new): A method of selectively eliminating target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

i) a DNA minor groove binding ligand incorporating a cytotoxically effective Auger electron emitting atom;

ii) a target cell specific protein or peptide that is capable of internalisation by the target cells;

wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

24. (new): A method of selectively eliminating target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

i) a DNA minor groove binding ligand incorporating a photoactive moiety which when photoactivated generates a species that induces cytotoxic DNA damage;

ii) a target cell specific protein or peptide that is capable of internalisation by the target cells;

and exposing the target cells to a source of UV light suitable to initiate formation of the species that induces cytotoxic DNA damage;

wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

25. (new): A method of selectively imaging target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

i) a DNA minor groove binding ligand incorporating a gamma-emitting and/or positron-emitting atom;

ii) a target cell specific protein or peptide that is capable of internalisation by the target cells;

and detecting and imaging gamma and/or positron emissions from the target cells;

wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

26. (new): The method according to any one of claims 23 to 25 wherein the cell targeting conjugate is administered to an ex-vivo population of cells.

27. (new): The method according to any one of claims 23 to 25 wherein the cell targeting conjugate is administered to a mammalian patient.

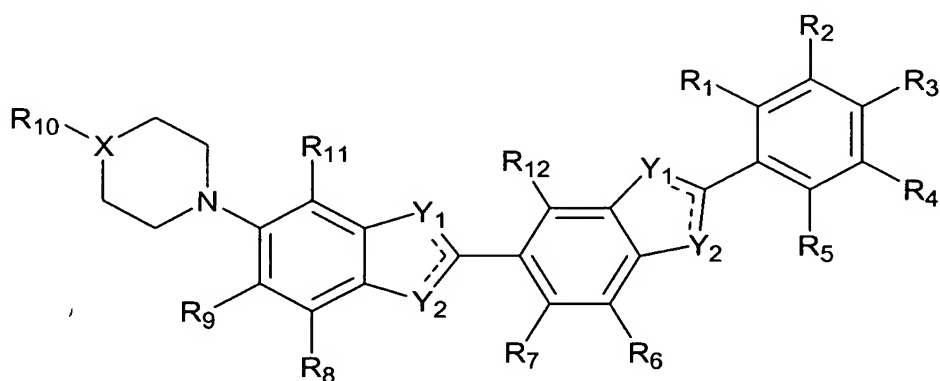
28. (new): The method according to any one of claims 23 to 25 wherein the target cells are tumour cells.

29. (new): The method according to any one of claims 23 to 25 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbix), BrE-3, murine A7, C50, humanized MN-14, anti-A33,

MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10), Campath-1H, N901, Ep2, somatostatin analogues, tositumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

30. (new): The method according to any one of claims 23 to 25 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

31. (new): The method according to any one of claims 23 to 25 wherein the cell targeting conjugate is represented by Formula (I), wherein:



Formula (I)

X is carbon or nitrogen;

Y_1 and Y_2 are selected from $C(R')$, nitrogen, $N(R')$, oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y_1 and Y_2 are not both either $C(R')$ or nitrogen;

\equiv is a double bond unless the attached Y_1 or Y_2 is $N(R')$, oxygen or sulfur in which case it is a single bond;

R_1 to R_{12} are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R_1 to R_5 may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R_1 to R_{12} comprises a target cell specific protein or peptide, and wherein at least one other of R_1 to R_{12} comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

32. (new): The method according to claim 25 wherein the gamma-emitting and/or positron-emitting atom is distanced from a DNA minor groove binding region of the conjugate.

33. (new): A compound according to Formula (I) wherein:

Y_1 and Y_2 are selected from $C(R')$, nitrogen, $N(R')$, oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y_1 and Y_2 are not both either $C(R')$ or nitrogen;

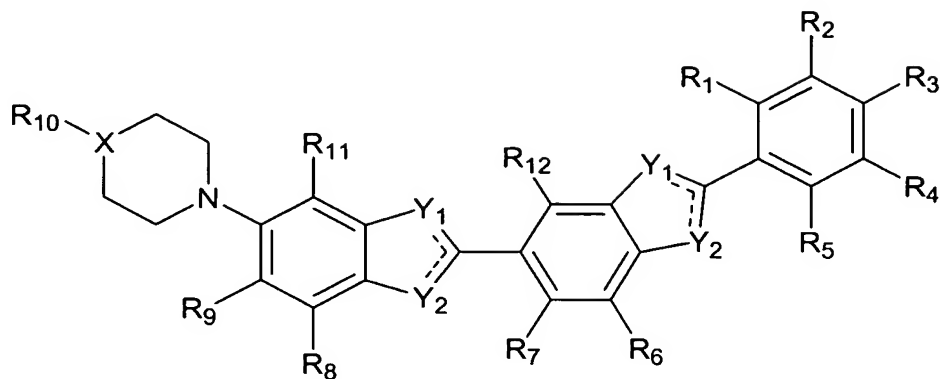
\equiv is a double bond unless the attached Y_1 or Y_2 is $N(R')$, oxygen or sulfur in which case it is a single bond;

R_1 to R_{12} are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R_1 to R_5 may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R_1 to R_{12} comprises a target cell specific protein or peptide, and wherein at least one other of R_1 to R_{12} comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

32. (new): The method according to claim 25 wherein the gamma-emitting and/or positron-emitting atom is distanced from a DNA minor groove binding region of the conjugate.

33. (new): A compound according to Formula (I) wherein:



Formula (I)

X is carbon or nitrogen;

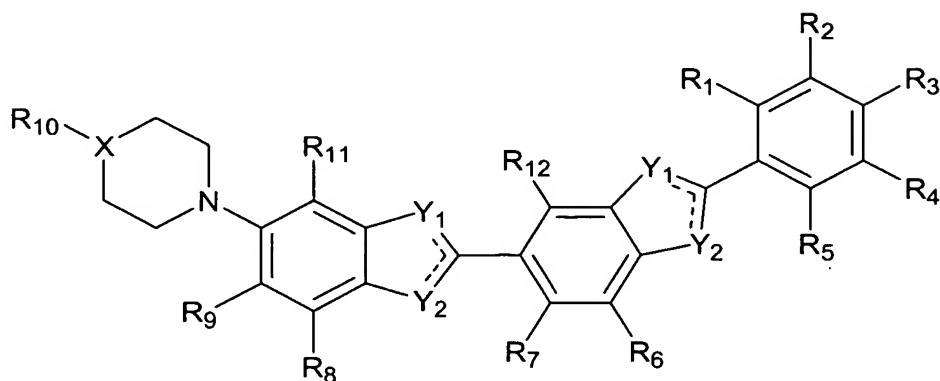
Y_1 and Y_2 are selected from $C(R')$, nitrogen, $N(R')$, oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y_1 and Y_2 are not both either $C(R')$ or nitrogen;

--- is a double bond unless the attached Y_1 or Y_2 is $N(R')$, oxygen or sulfur in which case it is a single bond;

R_1 to R_{12} are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a leaving group, a chelating group and a cellular uptake inhibiting group, and wherein two of R_1 to R_5 may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R_1 to R_{12} comprises a carbonyl, carboxylic acid or amino group, and wherein at least one other of R_1 to R_{12} comprises a leaving group or a chelating group;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

34. A compound according to Formula (I) wherein:



Formula (I)

X is carbon or nitrogen;

Y₁ and Y₂ are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y₁ and Y₂ are not both either C(R') or nitrogen;

--- is a double bond unless the attached Y₁ or Y₂ is N(R'), oxygen or sulfur in which case it is a single bond;

R₁ to R₁₂ are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R₁ to R₅ may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R₁ to R₁₂ comprises a carbonyl, carboxylic acid or amino group, and

wherein at least one other of R_1 to R_{12} comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.